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| STAPLES, MARK | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/558,277

Applicant(s)

CLELLAND ET AL.

Examiner

MARK STAPLES

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 55,56,90,93,97 and 104 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,6-8,12,13,15,16,25,39,40,42,45-50,64,65,78,79,85,86,88,105 and 106 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 February 2010 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims pending in the application are 2,6-8,12,13,15,16,25,39,40,42,45-50,55,56,64,65,78,79,85,86,88,90,93,97, and 104-106.

DETAILED ACTION

1. Applicant's amendment of claims 2, 45, 47, 49, 55, 56, 64, 85, 86, 88, 90, 93, 97, and 104; the cancellation of claims 1, 9, 10, 43, and 44; and the submission of new claims 105 and 106 in the paper filed on 02/23/2010 are acknowledged. Claims 55, 56, 90, 93, 97, and 104 remain withdrawn.

Claims 2, 6-8, 12, 13, 15, 16, 25, 39, 40, 42, 45-50, 64, 65, 78, 79, 85, 86, 88, 105 and 106 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections that are Moot / Withdrawn

Drawings

2. The replacement drawing was received on 02/23/2010. This drawing is acceptable.

Specification

3. The objection to improper indication of trademarks is withdrawn in view of Applicant's amendments to the specification to properly indicate trademarks.

Cancelled Claim Rejection Moot / Withdrawn

4. The rejections of cancelled claims 1, 9, 10, 43, and 44 are moot and therefore are withdrawn.

Claim Rejections Withdrawn - 35 USC § 102(b)

5. The rejection of claims 1, 2, 6-8, 39, 40, 42, and 45-50 under 35 U.S.C. 102(b) as being anticipated by Ralph et al. (US Patent No. 6,190,857 issued 2001) is withdrawn. Applicant's arguments with respect have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

Rejections that are Maintained

Claim Rejections Maintained - 35 USC § 102

6. The rejection of claims 2, 6-8, 12, 13, 15, 16, 25, and 45-50 under 35 U.S.C. 102(b) as being anticipated by Ilani et al. (2001) is maintained. Applicant's arguments have been fully considered but they are not persuasive. The rejection is given below.

Applicant argues that Ilani et al. does not teach two or more genes or transcribed nucleic acids. However, Ilani et al. specifically teach transcription of the total RNA from lymphocytes into first strand cDNA and specifically teach this contains at least two genes and at least three transcribed nucleic acids of D₃ dopamine receptor gene, D₄ dopamine receptor gene, and β actin gene (see 3rd paragraph on p. 626 continued to p. 627) and evaluating these nucleic acids. It is also noted that Ilani et al. teach the psychiatric disease which is schizophrenia (see Title). Thus the rejection is maintained.

Claim Rejections Maintained- 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 2, 6-8, 12, 13, 15, 16, 25,42, and 45-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Ilani et al. (2001).

Regarding claim 2, Ilani teaches methods for evaluating psychiatric disease which is schizophrenia of a subject (see abstract) which methods comprise comparing (i) an expression profile of surrogate cells from the subject (see Figure 1 and p. 626), with (ii) a normal expression profile of surrogate cells from a normal subject or subjects (see Figure 1 and p. 626), wherein a difference between the expression profiles of at least three transcribed nucleic acids of D₃ dopamine receptor gene, D₄ dopamine receptor gene, and β actin gene (see 3rd paragraph on p. 626 continued to p. 627) which is indicative of the physical state of the subject under investigation (see Figure 1 and p. 626).

With regard to claim 6, Ilani teaches human subjects (see p. 626 column 1).

With regard to claims 7 and 8, Ilani teaches the use of peripheral blood leukocytes encompassing monocytes, macrophages, etc. (see p. 626, column 1).

With regard to claims 12, 13, 15, 16, and 25, Ilani teaches detection and evaluation of patients for schizophrenia and Alzheimers (see p. 626, Figure 1, and p. 628 column 1).

With regard to claims 45-50, Ilani teaches diagnosis and prognosis and monitoring therapies using the method (see p. 628, column 2).

With regard to claim 42, Ilani also teaches reverse-transcriptase PCR, RT-PCR (see page 626, column 2).

Claim Rejections Maintained - 35 USC § 103

9. The rejection of claims 64, 65, 78, 79, 85, 86, and 88 under 35 U.S.C. 103(a) as being unpatentable over Kamizono et al. (U.S. Patent 6,248,533 issued 2001), Ralph et al. (US Patent No. 6,190,857 issued 2001), and Ilani et al. (2001) is maintained. Applicant's arguments have been fully considered but they are not persuasive. The rejection is given below.

Applicant argues that neither Ralph nor Kamizono teach the newly amended recitations of evaluating evaluating neurological, psychiatric or mood diseases or disorders. However, Ilani et al. teach evaluating a psychiatric disease as given above and as follows.

In response to applicant's argument that the Ilani et al. reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., (1) "connection" between expression of at least two genes and disease and (2) evaluating a gene with more statistical significance than another gene)

are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It is also noted that the D₃ dopamine receptor gene is but one of at least three nucleic acids in the expression profile which Ilani et al. evaluate. Ilani et al. also expressly teach that the expression and monitoring of two genes (which are multiple genes) of D₃ dopamine receptor gene and β actin gene in an expression profile ratio are used to evaluate the psychiatric disease which is schizophrenia (see Table 4).

Regarding claim 64, Applicant argues that Kamizono does not teach "the entire transcribed region, plus upstream and downstream controlling elements". However Kamizono teach expressing promoter regions in expression profiles of nucleic acids (see Figure 2-5, 6, 7, and Example 2). Furthermore, Ralph teaches expression constructs (see section 4.2.3.1 beginning in column 24) include regulatory controlling elements including upstream (see column 25 lines 34-39 and column 30 line 59) and downstream elements (see column 25 lines 34-39 for promoters containing both upstream and downstream elements) for evaluating diseases and disorders.

Claim Rejections Maintained - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 64, 65, 78, 79, 85, 86, and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamizono et al (U.S. Patent 6,248,533 issued 2001), Ralph et al. (US Patent No. 6,190,857 issued 2001), and Ilani et al. (2001).

Regarding claim 64, Kamizono teaches a methods for identifying a nucleic acid containing a sequence alteration that results in susceptibility to a physical state (see abstract) comprising: (a) selecting a nucleic acid that has altered expression in a surrogate cell from a subject with the physical state when compared to a surrogate cell from a normal subject or subjects (see column 11, table 7 regarding IDDM patients) and (b) comparing the genomic sequence of the nucleic acid including the transcribed region, wherein a sequence difference indicates that the nucleic acid alteration results in or contributes to susceptibility to the physical state (see column 11, table 7 and example 11). Kamizono also teach expressing upstream promoter regions in expression profiles

of nucleic acids (see Figure 2-5, 6, 7, and Example 2). Thus Kaminczono at least suggest expression profiles of entire transcribed regions, plus upstream and downstream controlling elements.

With regard to claim 65, Kamizono teaches linkage of the polymorphism to IDDM (see example 11 and table 7). Kamizano also teaches DNA analysis (see column 6, example 4) and human subjects (see column 12, example 11). Kamizano also teaches isolation from PBMC (see column 5, example 2). Kamizano also teaches the use of Biopsy specimens (see column 3, line 7).

With regard to claims 85, 86, and 88, Kamizano teaches diagnosis (see column 11, table 7 and abstract) and teaches a method of claims 1, 2, 43, and 44, for evaluating a physical state of a subject (see abstract) which method comprises comparing (i) an expression profile of surrogate cells from the subject (see column 5, lines 33-43 and see example 5), with (ii) a normal expression profile of surrogate cells from a normal subject or subjects (see column 5, lines 33-43 and example 5), wherein a the expression profiles is indicative of the physical state of the subject under investigation (see column 5, lines 33-60 and example 5).

Ralph teaches a method of claims 1, 2, 43, and 44, for evaluating a physical state of a subject (see abstract) which method comprises comparing (i) an expression profile of surrogate cells from the subject (see column 5, lines 33-43 and see example 5), with (ii) a normal expression profile of surrogate cells from a normal subject or subjects (see column 5, lines 33-43 and example 5), wherein a difference between the expression profiles is indicative of the physical state of the subject under investigation

(see column 5, lines 33-60 and example 5). Ralph also teaches analysis of risk or susceptibility to disease (see column 5, lines 3-7).

Regarding claim 64, Ralph teaches expression constructs (see section 4.2.3.1 beginning in column 24) include regulatory controlling elements including upstream (see column 25 lines 34-39 and column 30 line 59) and downstream elements (see column 25 lines 34-39, including promoters containing both upstream and downstream elements) for evaluating diseases and disorders.

With regard to claim 89-94, Ralph teaches treatment with gene therapy vectors and antisense (see columns 23 and 24).

Ralph teaches application to a variety of disease states but does not teach neurological disease states.

Ilani teaches a method of claims 1, 2, 43, and 44, for evaluating a physical state of a subject (see abstract) which method comprise comparing (i) an expression profile of surrogate cells from the subject (see figure 1 and page 626), with (ii) a normal expression profile of surrogate cells from a normal subject or subjects (see figure 1 and page 626), wherein a difference between the expression profiles is indicative of the physical state of the subject under investigation (see figure 1 and page 626).

With regard to claims 78 and 79, Ilani teaches detection and evaluation of patients for schizophrenia and Alzheimers (see p. 626, Figure 1, and p. 628 column 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the full scope of the Ralph method and the Ilani method in the method of Kamizano for therapeutic selection. The motivation to do so is provided by Kamizano who teaches that polymorphisms may be significantly associated with disease and the teaching of Ralph and Ilani of how to demonstrate disease associations. It would further have been obvious to apply the method of Kamizano to any disease known to be associated with surrogates as taught or suggested by Ralph and Ilani. Furthermore, both Kamizano and Ralph provide motivation to use expression profiles of entirely transcribed regions by teaching these regions contain important regulatory controls upstream and downstream which are involved in diseases and disorders, and Kamizano further teaches the importance of evaluating polymorphisms in upstream promoter regions. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

New Rejections Necessitated by Amendment

New Claim Rejections - 35 USC § 102

13. Claim 105 is rejected under 35 U.S.C. 102(b) as being anticipated by Ilani et al. (2001).

Regarding claims 2, 12, and 13, Ilani teach as noted above.

Regarding claim 105, Ilani teach where the neurodegenerative disease is Alzheimer's disease (see last paragraph on the 1st column on p. 628).

14. Claim 106 is rejected under 35 U.S.C. 102(b) as being anticipated by Ilani et al. (2001).

Regarding claim 106, Ilani teaches methods for evaluating psychiatric disease which is schizophrenia of a subject (see abstract) which methods comprise

(a) obtaining an expression profile of surrogate cells from the subject (see Figure 1 and p. 626), and

(b) obtaining a normal expression profile of surrogate cells from a normal subject or subjects (see Figure 1 and p. 626),

(b) comparing the expression profiles of (a) and (b) of at least three transcribed nucleic acids of D₃ dopamine receptor gene, D₄ dopamine receptor gene, and β actin gene (see 3rd paragraph on p. 626 continued to p. 627) , and

(c) identifying the subject as having the psychiatric disease which is schizophrenia (see Title).

15. Claim 106 is rejected under 35 U.S.C. 102(b) as being anticipated by Ilani et al. (2001).

Regarding claim 106, Ilani teaches methods for evaluating psychiatric disease which is schizophrenia of a subject (see abstract) which methods comprise

(a) obtaining an expression profile of surrogate cells from the subject (see Figure 1 and p. 626), and

(b) obtaining a normal expression profile of surrogate cells from a normal subject or subjects (see Figure 1 and p. 626),

(b) comparing the expression profiles of (a) and (b) of at least three transcribed nucleic acids of D₃ dopamine receptor gene, D₄ dopamine receptor gene, and β actin gene (see 3rd paragraph on p. 626 continued to p. 627) , and

(c) identifying the subject as having the psychiatric disease which is schizophrenia (see Title).

New Claim Rejections - 35 USC § 103

16. Claims 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ilani et al. as applied to claim 2 above, and further in view of Ralph et al. (US Patent No. 6,190,857 issued 2001).

Ilani teach as noted above.

With regard to claims 39 and 40, Ralph teaches cDNA on nylon or nitrocellulose membranes which represent cDNA microarrays (see column 16, lines 29-50).

And similar to Ilani regarding claims 2, 6-8, 25, and 45-50, Ralph also teaches methods for evaluating a physical state of a human subject (see abstract and column 89, lines 30-67) which methods comprise comparing (i) an expression profile of surrogate cells which are peripheral blood leukocytes encompassing monocytes, macrophages, etc. (see column 89, lines 30-67) from the subject (see column 5, lines 33-43 and see example 5), with (ii) a normal expression profile of surrogate cells from a normal subject or subjects (see column 5, lines 33-43 and example 5), wherein a difference between the expression profiles is indicative of the physical state of the subject under investigation (see column 5, lines 33-60 and example 5). Ralph also

teaches treatment with gene therapy vectors and antisense (see columns 23 and 24). With regard to 25, Ralph teaches detection of breast and prostate cancer (see column 89, lines 28-30 and example 5). With regard to claim 42, Ralph teaches RT-PCR (see column 54, lines 1-7). With regard to claims 45-50, Ralph teaches diagnosis and prognosis and monitoring therapies using the method (see column 5, lines 44-47). Ralph also teaches analysis of risk or susceptibility to disease (see column 5, lines 3-7). Ralph further teaches testing a biochemical marker of the physical state in blood (see column 89, example 5). In addition, Ralph teaches biopsy as a comparison (see column 89, lines 59-61).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Ilani for comparing expression profiles by using a microarray for comparing expression profile as suggested by Ralph with a reasonable expectation of success. The motivation to do so is provided by Ralph who teach that microarrays permit the assembly of large libraries of cDNA for evaluating diseases. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

17. No claim is free of the prior art.
18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Staples/
Primary Examiner, Art Unit 1637
05/19/2010